CLINICAL ASPECTS OF CARCINOMA OF STOMACH IN DIAGNOSIS

BASED UPON THE STUDY OF 146 CASES*

BY

JOHN GILMOUR, M.S., F.R.C.S.

Surgeon, Royal Victoria Infirmary, Newcastle upon Tyne

The clinical diagnosis of gastric carcinoma, with its subsequent treatment, remains one of our most challenging problems. Its magnitude may be gauged from the fact that the stomach is the commonest site of malignant disease. Fully 40% of gastro-intestinal cancers occur in the stomach. It accounts for one-third of all cancers in men and for one-fifth in women, and 15,000 persons die annually of the disease in Great Britain. Again, whilst it is true that modern surgical management has extended the range of operative treatment to over 50% of its sufferers, and has reduced the immediate mortality rate, it is still lamentably true that only about 10% survive resection for five years or over. The important point here is that these are patients in whom lymphatic spread is either absent or very strictly localized.

The trend of modern thought is therefore to consider how to establish the diagnosis at a earlier stage in the disease process. This will depend upon a better appreciation of the clinical features of early carcinoma, a greater knowledge than we at present possess of the pre-cancerous states of the stomach, and the reliance which the radiologist, the gastroscopist, and the cytologist can inspire by the accuracy of their reports in early cases. The primary responsibility for singling out the patient with suspicious symptoms of gastric cancer remains with the family doctor, and the surgeon whom he consults should be prepared to admit the patient without delay for study and investigation.

Present Series

Gastric carcinoma is a disease of adult life. Table I shows the age and sex incidence in a series of 146 patients with gastric carcinoma dealt with in my wards at the Royal Victoria Infirmary. Of these, 70% had no previous history of ill-health, but their symptoms ranged from a few weeks to one year, with an average duration of between five and six months; 15% had dyspeptic histories of one to five years, and 15% had had stomach trouble for many more years. In the majority, therefore, we are confronted by an adult

TABLE I.—Age and Sex Incidence

Ages					Males	Females	Total
30-39	..	..	..	..	3	2	5
40-49	..	..	..	..	16	4	20
50-59	..	..	..	..	35	15	50
60-69	..	..	..	..	34	12	46
70-79	..	..	..	..	19	4	23
80-89	..	..	..	..	—	2	2
Total	..	..	..	..	107	39	146

Youngest male, 34. Youngest female, 38. Oldest male, 79. Oldest female, 85.

patient suffering from his stomach for the first time, but in a large minority there is a previous gastric history which requires the closest attention.

The problem of gastric carcinoma is complicated because the disease may originate at any part. In my series the distribution was: pyloric segment, 44%; lesser curvature, 14.7%; body, 29.3%; cardia, 12%. Again, it occurs in several forms, and Borrmann's classification (Table II) is a useful reminder.

*Read in the Section of Surgery at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

The signs and symptoms naturally vary with the site of the growth, its extent, and its type; but there are three overriding factors which are primarily responsible for the symptoms, and the resulting clinical features of any one case are due to one or more of these factors. These are: (1) the constitutional or toxæmic effects of the growth; (2) the effects of its ulceration upon the individual; and (3) the mechanical effects of carcinomatous infiltration of the gastric musculature or obstruction of its orifices or lumen.

TABLE II.—Pathological Types—Incidence

1. Polypoid Tumours. Single, of low malignancy; infiltrate late; bleed readily, causing anaemia	7.5%
2. Localized Carcinomatous Ulcers. Infiltrate slowly—clearly defined edge	21.0%
Ulcer-cancers	14.6%
3. Ulcerating Infiltrating Carcinomas. Spread and disseminate quickly, advancing edge beyond ulcerated surface	23.0%
4. Diffuse Non-ulcerating Carcinomas:	
Localized form as a plaque, annular or conical growth	23.0%
Linitis plastica; leather-bottle stomach	10.8%
Spread slowly and infiltrate widely; disseminate by lymphatics late.	

Constitutional or Toxæmic Effects

The constitutional or toxæmic effects of a carcinoma are due to its metabolites and are most pronounced in cellular growths which proliferate, infiltrate, and disseminate rapidly, whilst they are less marked in the more localized carcinomatous ulcer, ulcer-cancer, and fibrotic scirrhous.

The following are most likely to attract early attention: (a) *The fatigue syndrome*, in which general lassitude, malaise, and mental apathy are the chief symptoms. (b) *Anorexia*, which is commonly present, particularly when there is hypochlorhydria or achlorhydria, and which progresses until there is repugnance for food and particularly for meat. However, in ulcer-cancers with free hydrochloric acid in the gastric juice appetite may be retained. (c) *Loss of weight*. This is important: it is usually gradual but persistent, though it becomes rapid when there is either pyloric or cardiac obstruction. (d) Development of a tendency to constipation. (e) A relatively low blood pressure: this is a frequent feature.

In my series there were six cases in which toxæmic symptoms predominated. These were patients with marked fatigue and loss of appetite who had large inoperable growths in the middle segment of the stomach.

Effects of Ulceration of Growth

Ulceration of the growth may result in (1) occult haemorrhage—anaemia; (2) overt haemorrhage; or (3) perforation.

1. Ulceration commonly causes a chronic loss of blood as this drips from the surface. In addition, protein, electrolytes, and fluid escape from the ulcer, and a secondary anaemia of the hypochromic microcytic type develops which will respond temporarily at least to iron treatment and blood transfusion. Pallor, dyspnoea or exertion, giddiness, and exhaustion may therefore be the primary sign of a "silent" carcinoma or may develop as a complicating condition in a dyspepsia due to carcinoma. Mention should be made of three other types of anaemia which may occur in gastric cancer. There may be hyperchromic megaloblastic anaemia—that is, Addisonian in type—when the growth has destroyed the source of the intrinsic factor, or a true pernicious anaemia in which a general atrophy of the body mucosa is associated with a carcinoma. Treatment with vitamin B₁₂ will restore the blood picture in both instances. Finally, there may be a leuco-erythroblastic anaemia due to a fine widespread dissemination of cancer cells throughout the bone marrow, and this, of course, is an irreversible condition: destruction of the supply of blood platelets may result in a purpuric rash. The key to the problem of unexplained anaemia lies, therefore, in a blood examination and in the

discovery of occult blood in the stools. Of the 20 cases in which anaemia was the primary condition and ulcerating lesions or polypoid growths were responsible, 14 were resectable.

2. *Overt Bleeding*.—Haematemesis and melaena are commonly regarded as complications of acute or chronic peptic ulceration, but it is important to remember that occasionally a severe haemorrhage may come from a carcinoma. This happened in 12 cases and accelerated admission to hospital in five of them. Its earlier occurrence in patients with long histories of gastric trouble is apt to be misleading, for in such it is easy to forget that the latest haemorrhage may have a carcinomatous origin. The importance of discovering its source needs no emphasis; the same applies when the vomit has a coffee-grounds appearance.

3. *Acute perforation* of a carcinomatous ulcer is rare. It occurred in six cases; two were in early growths and both were resected. In a suspicious perforation a biopsy or immediate partial gastrectomy should be done. It is interesting to record that one of those patients is alive and well after nearly 10 years. Subacute perforation also occurs, and may result in a localized abscess. Late in the disease it may cause a septic peritonitis to be superimposed upon a carcinomatous peritonitis with ascites.

Mechanical Effects of Carcinoma

The mechanical effects of a carcinoma are due either to local muscular infiltration or to obstruction of one or other orifice or lumen. When local infiltration occurs the affected segment of the stomach wall can neither relax during gastric filling nor contract when peristalsis occurs. Dyspeptic symptoms result which may be mild to begin with, but which increase in severity and in duration as the growth extends, until pain is continuous and occurs also at night. This must be due to the increasing embarrassment caused by the growth and the greater peristaltic effort required to empty the stomach. At the same time emptying tends to be incomplete and vomiting ensues until in some cases with retention it occurs at four- to six-hourly intervals.

It is noteworthy that dyspeptic symptoms are most pronounced when the growth lies on the "gastric canal"—that is, the lesser curvature, the pyloric antrum, and canal, the area of deep peristalsis—and that symptoms are less marked when the weaker musculature of the fundus body or upper half of the greater curvature is involved.

Thus the site of infiltration is more important than the type of growth. This explains why different types of growth may produce the same symptoms and why the same type of growth may cause different symptoms in two patients.

In practice the dyspeptic symptoms of carcinoma have a distinct time relationship to the gastric cycle, and if those of obstruction are added we can recognize five primary types: filling dyspepsias, pyloric mill syndrome, gastric ulcer syndrome, duodenal ulcer syndrome, and obstructive syndromes.

Filling Dyspepsias

The filling dyspepsias are characterized by the onset of symptoms during or immediately after food, with aggravation by more food, and relief from vomiting. The first symptom is often a sense of fullness after eating. In time this becomes a discomfort, later an ache, and finally a pain. Sometimes the primary complaint is of flatulence at table with relief from belching. Occasionally there is nausea without pain. It may occur before breakfast or follow a meal. Vomiting will always relieve it.

Again, the only symptom may be a sudden attack of vomiting during or after food. This may point to an early pyloric or cardiac obstruction. As a late symptom vomiting usually follows pain. Such an attack may recur, and is apparently due to local spasm or oedema at the orifice set up by the growth. Its significance should not be overlooked, for it heralds the approach of a more complete malignant obstruction. When the growth is on the fundus or body the

first symptom may be the inability to complete a full meal, or a sense of fullness after a small meal. The late picture may therefore be that of a filling dyspepsia complicated by loss of appetite and weight and some degree of anaemia.

Filling dyspepsias are relatively common in gastric cancer because they arise with growths on the lesser curve and pyloric segment of the stomach. In my series 35 patients had this syndrome, and milder dyspepsias of this type occurred in 14 out of 26 patients whose primary complaint was of anaemia or exhaustion.

Pyloric Mill Syndrome

A few patients insist that their symptoms began about a quarter of an hour after food and might last for periods of up to an hour. They had discomfort or pain aggravated by food and relieved by vomiting, which frequently occurred. Alkalis might also ease the pain. They became afraid to eat. Their complaints are therefore similar to those with filling dyspepsias but differing by the short period of freedom after a meal. Naturally if they had a filling dyspepsia instead, followed by vomiting, they could not develop a pyloric mill syndrome, which coincides with the onset of digestive gastric activity. The causal lesion lies on the lesser curvature and the pyloric antrum, but not in the pyloric canal. There were eight examples in my cases, and in one the growth lay high on the lesser curve.

This syndrome differs from that of a chronic gastric ulcer by the shorter interval of freedom from pain after food; by the fact that food immediately aggravates and does not relieve the pain; and by the greater frequency of vomiting in the early stages. On the other hand, the relief from alkalis will tend to confuse the diagnosis.

Gastric Ulcer Syndrome

In the gastric ulcer syndrome of carcinoma there is pain one to two hours after food, with relief from more food, from alkalis, and from vomiting when it occurs. These symptoms are naturally a fruitful source of confusion and delay in diagnosis. There are other difficulties. (1) The improvement obtained from bed rest and lavage in gastric ulcer may also be seen in carcinoma, when this can be attributed to the alleviation of the associated chronic gastritis. (2) Though a scirrhus carcinoma may be the cause of the symptoms, ulcer-cancers and localized carcinomatous ulcers are the commoner causes and there may be some difficulty in differentiating them from chronic ulcer. (3) In about 30% of those with ulcer symptoms the clinical history may extend over several years and simulate simple ulcer. (4) In cases of ulcer-cancer, as in simple ulcer, there is often free hydrochloric acid in the gastric juice and a good appetite is retained.

The danger lies in persevering with medical treatment too long on the assumption that the ulcer is simple. Malignancy is to be feared when the ulcer is prepyloric, or occurs on the greater curve, in any case when there is achlorhydria, when relief from food and alkalis grows less and vomiting becomes more frequent, and when the pain loses its periodicity. In ulcer-cancers the symptoms may change dramatically—the pain becomes less severe but more constant, and vomiting gives shorter relief. Appetite may suddenly disappear. Additional help is got by finding occult blood frequently in the stools or when the vomit becomes foul-smelling and has the appearance of coffee grounds. Clinically the absence of the "deep tender spot" of a chronic ulcer and the possible presence of a palpable lump are significant.

All cases with the ulcer syndrome should be admitted for investigation. If a positive diagnosis cannot be made the patient should be retained in hospital under medical treatment for two to three weeks and then reinvestigated thoroughly. In case of further doubt a surgical resection is amply justified. Opinions differ about the percentage of chronic ulcers which become malignant. In 168 resected carcinomas at the Royal Victoria Infirmary, 13.7% were

histologically proved ulcer-cancers, and in my own series the percentage was 14.6. Again, it is frequently stated that in 15% of carcinomas there is a previous history of peptic ulcer.

Of the 31 patients in my series with this syndrome only 14 were resectable—a clear indication for an earlier and more exact investigation of the group.

Duodenal Ulcer Syndrome

The duodenal ulcer syndrome of carcinoma deserves to be better known, for the pain occurs two to three hours after food, is often a true "hunger pain," and is relieved by food and by alkalis. Vomiting is infrequent. It occurs when the stomach is contracting down, and is associated with lesions on the pyloric canal and the adjacent parts of the antrum and lesser curve. These are commonly ulcer-cancers, local carcinomatous ulcer, and occasionally a scirrhus or a polyp. Sometimes the pain is spasmodic or colicky, as if the stomach were attempting to expel the growth.

The importance of recognizing this syndrome in gastric carcinoma lies in the fact that the treatment of uncomplicated duodenal ulcer is medical and that such measures afford relief in carcinoma by diminishing the associated gastritis. Only 8 of the 14 examples of this syndrome in my series were resectable.

Chronic atrophic antral gastritis is another condition which simulates duodenal ulcer during an exacerbation, but it may also show some of the features of a carcinoma, as there may be anorexia, loss of weight, achlorhydria, and occasionally occult blood and some anaemia. Considerable attention is being centred upon this condition to-day as the result of cytological studies, and its position as a premalignant state is attracting a fresh study, as are the works of Konjetzny, of Hurst, and of Faber, who propounded this view nearly 30 years ago. The need to investigate patients carefully with this syndrome requires no further argument.

Combined Dyspepsias.—In the later stages of the disease some patients complain of both a filling and an emptying dyspepsia. There is usually some immediate symptom on eating, such as nausea, fullness, or discomfort eased by belching, by alkalis, or by vomiting; an hour or two later the patient complains of a hunger pain, for which he feels he must eat. When he does the cycle of dyspepsia starts over again. He is therefore apt to complain that he gets pain with or without food—or at any time. There were six examples of this combination in the series: two leather-bottle stomachs; two diffuse carcinomas of pyloric antrum and body; one diffuse carcinoma of lesser curve accompanied by a malignant polyp on the greater curvature; and one localized scirrhus in the pyloric canal. It will be noted that in the last condition encroachment upon the pyloric sphincter set up both a filling and a duodenal type of dyspepsia and that in the other five instances the growths were extensive.

Obstructive Syndromes

Obstructive lesions are never found in the early stages of the disease. Stenosis at the pylorus or cardia may certainly develop insidiously, but in the majority there is a prodromal dyspepsia. Where such is absent the first sign of obstruction may be an attack of vomiting, and this should always receive particular attention. Visible peristalsis in the epigastrium should be looked for, and a lump may be felt. In the series there were eight examples of pyloric stenosis and five were resectable.

Dysphagia is usually described as the cardinal symptom of stenosis at the cardia. This is misleading. In 17 examples only seven patients complained initially of dysphagia; in nine there was a preliminary dyspepsia lasting from 3 to 12 months; and one had had stomach trouble for five years before his dysphagia appeared. Two patients were admitted with haematemesis, two had troublesome hiccup, and one had a fixed pain in the left hypochondrium. In no case

had the growth extended down from the lower oesophagus, though this of course is a possibility. The lesson is that the cardia may become stenosed by a growth at that site or by the upward extension of a growth from the neighbouring parts of the stomach.

In hour-glass stenosis and in *linitis plastica* pain and the regurgitation of food may also follow in the course of a meal. It is therefore necessary to know whether the lesion is in the lower oesophagus, the cardia, or the upper part of the stomach and whether the oesophageal wall is free from secondary deposits. Cardiac growths appear to be relatively favourable for surgery so long as the liver and oesophagus are not involved. Eleven of the 17 cases were found to be operable. They appear to be of the less-malignant types. In a recent experience a local recurrence in the lower oesophagus four years after a total gastrectomy proved to be resectable.

Other Symptoms

Unusual symptoms may lead the clinician astray. Pains referred from the stomach posteriorly should not be mistaken for muscular strain or rheumatism or spinal arthritis. Pains referred to the left or right flank having a close relation to food should not be confused with pain originating in the colon simply because there is increasing constipation. Colicky spasms originating in the stomach spread from left to right and should be distinguished from those of the transverse colon. A fixed pain in the left hypochondrium which is aggravated by food is not of renal origin. It is usually gastric and calls for investigation. Persistent hiccup may be a significant symptom.

Physical Signs

Wasting and anaemia, gastric peristalsis in pyloric stenosis, and the possible presence of an epigastric lump are all the physical signs that may be found in operable cases. The mobility of the gastric tumour is important, but of course only those in the lower half of the stomach can be felt. This may be difficult if the stomach is empty, but with a full stomach it may be easier, particularly on deep inspiration or with the patient erect. The lump of an early carcinoma is usually painless on palpation and so differs from the "ulcer-tumour" of a chronic peptic ulcer, which is tender and may diminish in size under medical treatment within a few weeks.

The odd patient may be encountered who announces that he has a lump in his stomach but no other complaints. The prognosis need not be hopeless, for 27 out of 50 palpable carcinomas were found to be operable.

Signs of Dissemination

Epigastric tenderness and guarding generally mean peritoneal involvement in the gastric field, and all the other physical signs found later in the disease arise from its dissemination. These include: (1) Distant lymphatic metastases—in the left supraclavicular region, the left axilla, or groins. (2) Liver enlargement from secondary deposits or with obstructive jaundice from lymphatic metastases in the portal fissure. (3) Transperitoneal pelvic deposits found on rectal examination: (a) the rectal shelf of Shenton or (b) Krukenberg's bilateral ovarian tumours. (4) Ascites or left pleural effusion. (5) Carcinomatosis peritonei with or without intestinal obstruction. (6) The hard umbilical nodule or other skin nodules. (7) Pyrexia from widespread disease. (8) Cachexia—possibly with diarrhoea. (9) The secondary involvement of other organs such as lung, bone, spine, and brain.

Associated Gastric Lesions

A brief glance at the records of those with long histories shows that, whilst in some the carcinoma may have developed slowly, in others there is an interesting background of previous stomach trouble in which there has often been a recent change in the symptoms. Such patients include cases of gastric and duodenal ulcer, of recurring gastritis with or without bleeding, or haematemesis treated at home, of gastro-enterostomy for duodenal ulcer, and of recurrent

carcinoma in the gastric stump—the occurrence of such cases 3½, 7, and 17 years after a partial gastrectomy for cancer suggests a new malignancy.

In addition there were cases with a double pathology such as gastric or duodenal ulcer with carcinoma; chronic gastritis, simple polyp and cancer; simple and malignant polyp; and malignant polyp and infiltrating carcinoma. These lend force to the dictum of Hurst that gastric carcinoma never develops on a normal mucosa.

Conclusion

The emphasis in an earlier clinical diagnosis is upon symptoms, and the taking of a careful clinical history is the first step. Once the suspicion of malignancy is aroused in the mind of the surgeon and investigations are begun, he must be wary of the negative report, for this in the past has led to disaster. Fortunately he can now rely upon three lines of scientific investigation—namely, radiology, gastroscopy, and cytology—and by sifting the evidence they provide he may reasonably hope to advance the detection of this disease and thereby to improve the prospect of cure which only surgery can offer.

PROSTATITIS AND ANKYLOSING SPONDYLITIS

BY

R. M. MASON, D.M., M.R.C.P.

R. S. MURRAY, M.D., F.R.C.S.I., D.M.R.

J. K. OATES, M.B., B.S., M.R.C.P.Ed.

AND

A. C. YOUNG, M.B., B.S., D.M.R.D.

From the London Hospital

As part of a study of the radiological appearances of Reiter's disease two groups of patients, one with ankylosing spondylitis and one with rheumatoid arthritis, have been used for comparison. Since it has been argued that (1) Reiter's disease is a variant of rheumatoid arthritis (Littler, 1951), (2) ankylosing spondylitis is a variant of rheumatoid arthritis (Committee of American Rheumatism Association, 1953), (3) ankylosing spondylitis is a complication of Reiter's disease (Ford, 1953), and (4) ankylosing spondylitis is due to genital infection (Romanus, 1953), it was clearly necessary to determine the incidence of genital inflammatory disease in the two latter groups. All cases were therefore examined for signs of chronic prostatitis. We were impressed with the frequency with which patients with ankylosing spondylitis were found to have this condition when compared with those suffering from rheumatoid arthritis, the incidence being almost as high as that found in patients with Reiter's disease. We have therefore examined the data with particular care to ensure that this finding is not due to some other unrelated factor or to misdiagnosis. The present report covers this part of the investigation alone, and the radiological findings are discussed only to the extent that they relate to this aspect.

TABLE I.—Clinical Material—Age at Time of Study

	Age in Years												Total	Mean Age (Years)	Mean Duration (Years)	Mean Age of Onset (Years)
	15-		25-		35-		45-		55-		65-					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%				
Ankylosing spondylitis ..	9	17	10	19	25	46	6	11	4	7	0	0	54	37.4	10.1	27.3
Rheumatoid arthritis ..	0	0	5	6	15	17	29	34	26	30	11	13	86	52.7	6.7	46.0
Reiter's disease ..	6	10	12	20	11	19	25	42	4	7	1	2	59	42.2	8.4	33.8

Clinical Material

Fifty-four cases of ankylosing spondylitis were studied and compared with 86 cases of rheumatoid arthritis and 59 of Reiter's disease, all males, a total of 199 cases. Those with ankylosing spondylitis and rheumatoid arthritis presented to the Department of Physical Medicine and Regional Rheumatism Centre of the London Hospital, and those with Reiter's disease mostly to the Whitechapel Clinic. We have included in the ankylosing spondylitis group only those cases in which a confident clinical diagnosis had been made, and have excluded all those in which reasonable doubt existed—for example, cases which might be classified as atypical spondylitis by Sharp and Easson (1954) and Sharp (1957). All the patients with rheumatoid arthritis were well-established typical cases. The diagnosis of Reiter's disease was based on the finding of a non-gonococcal urethritis associated with an arthritis of acute onset and a variable, often chronic, relapsing course. Conjunctivitis occurred in 24 of the 59 cases (40%) and uveitis and keratoderma blennorrhagica in 6 cases (10%) each.

Age Distribution and Disease Duration.—Each group presented a distinct frequency distribution of age at the time of study (Table I), the mean age of the ankylosing spondylitis group being 37.4 years, with a mean duration of disease of 10.1 years; the rheumatoid arthritis group had a mean age of 52.7 years, with a mean duration of 6.7 years; and the Reiter's disease group a mean age of 42.2 years, with a mean duration of 8.4 years. Disease duration was estimated from the first joint or spinal symptom in all categories.

Rose-Waaler Test

A Rose-Waaler test was carried out in 80% of the ankylosing spondylitis group, in all but one of the patients with rheumatoid arthritis, and in 34% of those with Reiter's disease. The technique used was that originally described by Waaler (1940) and Rose *et al.* (1948). Later modifications have given a higher degree of sensitivity to this test, but were not used for this study because of the additional time required for these techniques, time which a laboratory in a general teaching hospital could not allocate. The results (Table II) do, however, show a clear distinction

TABLE II.—Results of Rose-Waaler Test

	Positive		Negative		Test Not Done	
	No.	%	No.	%	No.	%
Ankylosing spondylitis ..	0	0	43	80	11	20
Rheumatoid arthritis ..	30	35	55	64	1	1
Reiter's disease ..	0	0	20	34	39	66

between the rheumatoid arthritis group on the one hand and the ankylosing spondylitis and Reiter's disease groups on the other. 35% of the rheumatoid arthritis group (38% of those with a history of one year or more) gave a positive Rose-Waaler test at the 1/16 level, while there were no positive titres in the other two groups. The incidence of positive tests in the rheumatoid group is comparable to that of Miller *et al.* (1949), who obtained 33%, using a similar technique. An analysis of the sample of ankylosing spondylitis and of Reiter's disease on which the test was done shows that these were reasonably homogeneous samples in terms of disease duration, the mean duration of the ankylosing spondylitis sample being 10.0 years and of Reiter's disease 6.2 years.